REMARKS

Reconsideration is requested.

Claims 9 and 21 have been canceled, without prejudice. Claims 1-8, 10-20 and 22-31 are pending. The claims have been amended to advance prosecution. No new matter has been added.

A Statement regarding the Interview Summary mailed September 15, 2003, was filed September 29, 2003.

Method claims 32-43, 47-48 and 50 have been amended in a manner similar to claim 1 and rejoinder and allowance of the method claims upon allowance of the product claims are requested. The Examiner is requested to provide a further opportunity to further amend the method claims, as may be required, to allow for rejoinder and allowance of the method claims with the product claims. Claim 49 has been amended to provide a product which the applicants submit should be included with the examination of claims 1-31, which define the Examiner's Group I.

Claim 9 has been canceled, without prejudice, to obviate the Rule 75 objection of claims 9 and 21 noted on page 2 of the Office action dated September 4, 2003. Withdrawal of the objection is requested.

To the extent not obviated by the above amendments, the Section 112, second paragraph rejection of claims 9, 11-12, 21, 24, 27 and 29 is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following.

(a) Claim 9 has been canceled, without prejudice.

(b) Claims 11 and 12 have been amended above to advance prosecution, in response to the Examiner's concerns. Claims 11 and 12 are submitted to be definite.

(c) Claim 21 has been canceled, without prejudice.

(d) Claim 24 has been amended to clarify that the site of attachment of the label differs between each of the sensing element and the variants thereof. This is explained on page 22 of the application.

(e) Claim 27 has been amended to introduce the full names of the previously abbreviated compounds.

(f) Claim 29 has been amended to specify that the binding proteins are odorant binding proteins from mammalian or insect olfactory organs.

The claims are submitted to be definite and withdrawal of the Section 112, second paragraph, rejection is requested.

The Section 102 rejection of claims 1-3, 20 and 25-27 over Gold (U.S. Patent No. 6,242,246) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

The applicants submit that Gold is concerned with a nucleic acid ligand biochip in which one or more specific nucleic acid ligands is attached to a solid support in a spatially defined manner. Each ligand binds specifically to a particular target molecule in a test mixture and the binding is determined by a detectable change at each specific location on the biochip.

Claim 1 of the present application however specifies that the biological sensing elements are polypeptides or fragments, truncations, domains or concatenations thereof. A biochip in which the "ligand" of Gold (equivalent to the biological sensing element of the present application) is other than nucleic acid and, more specifically, is a polypeptide, is not disclosed in Gold. The present claims therefore, which recite similar

details as claim 1 or are dependent there from, are submitted to be novel over Gold. Withdrawal of the Section 102 rejection over Gold is requested.

The Section 102 rejection of claims 1-5, 9-10, 13-14, 20-21, 25 and 28-31 over Reed (U.S. Patent No. 6,492,143), is traversed. The Section 102 rejection of claims 6-8 over Reed "as defined by Dal Monte (Chemical Senses, 1993, 18(6):713-721)" is traversed. Reconsideration and withdrawal of the Section 102 rejections based on Reed are requested in view of the following distinguishing remarks.

The applicants submit that Reed discloses a library of olfactory receptor odorant/ligand binding domains and methods of making and using said library. The Examiner makes particular reference to column 32 of Reed, stating that the assay described at lines 50 onwards uses an array that allegedly anticipates claim 1 of the present application.

This is respectfully disputed. The noted reference in Reed, is submitted to provide a description of the expression in a cell of cloned olfactory receptors with G protein subunits. Target compounds are then introduced and binding of the target compound to the receptor is measured by detection of an increase in intracellular calcium.

A first point of distinction between the system of Reed and the array of the present application is that the biological sensing elements of Reed (i.e., the expressed olfactory receptors) are not "discretely immobilised onto or within a solid support" as is required by, for example, claim 1 of the present application.

A second point of distinction between the system of Reed and the array of the present application is that the biological sensing elements of Reed (i.e., the expressed

olfactory receptors) do not have attached thereto a detectable label. As explained in column 32, detection is of an increase in cellular calcium using a particular dye and radiofluorometric imaging. The Examiner states that "the cells [of Reed] contain both the expression vector and fluorescent dye whereby the sensing elements are attached to the dye via being contained within the same cell". See, page 5 of the Office Action dated September 4, 2003. The applicants believe that, with due respect, the Examiner's interpretation of the cited art is not consistent with the interpretation one of ordinary skill in the art would give to the word "attached". The applicants believe that there is nothing in Reed to suggest that the expressed olfactory receptors (equivalent to the biological sensing elements of the present application) are attached to the dye – but rather that the dye is added to the cell solely to detect an increase in cellular calcium.

The claims are submitted to be patentable over Reed and withdrawal of the Section 102 rejections based on the same is requested.

The Section 103 rejections of claims 11-12, 15-19 and 22-24 over Reed in view of Hoffman (U.S. Patent No. 5,998,588), and claims 26 and 27 over Reed in view of Gold, are traversed. Reconsideration and withdrawal of the rejections are requested in view of the following distinguishing remarks.

The deficiencies of Reed have been described above and the same are not cured by either Hoffman or Gold. Consideration of the following in this regard is requested.

Hoffman is concerned with molecular conjugates for use in affinity separations, drug delivery and other bioengineering applications. As is stated in column 3 of Hoffman, conjugates are made comprising stimuli-responsive compounds bound to

interactive molecules at a specific site so that the stimulus-responsive component can be manipulated to alter ligand binding at an adjacent ligand binding site. The result of this is that ligand binding can be completely blocked or partially blocked or may allow un-binding of bound ligand, thereby allowing precise control of molecular interactions.

The starting point for Hoffman is thus clearly distinct from that of the present application. Whereas Hoffman is concerned with labeling a biological sensing element to manipulate ligand binding, the present application is concerned with labeling a biological sensing element simply to detect ligand binding.

In a typical example of ligand separation using the Hoffman system, stimulus-responsive components are attached to an interactive molecule at a particular site within the interactive molecule. Ligand is passed over the system and allowed to bind. Unbound ligand is thereby removed. Bound ligand is then removed for analysis or whatever by detachment from the interactive molecule. Detachment is brought about by introducing the stimulus to which the stimulus-responsive component is sensitive. Introduction of the stimulus causes the stimulus-responsive component to alter in such a manner as to cause the structure of the interactive molecule to change, thereby causing detachment of the bound ligand.

The applicants submit that the system of Hoffman is entirely different from that described in the present application, whereby broad specificity polypeptide sensing elements and variants thereof are attached to a solid support and have a detectable label attached thereto. Exposure to ligand results in a certain amount of ligand binding to the elements/variants, which is detected by a change in the characteristics of the label. The change in the characteristics of the label is brought about by ligand binding

and not by the introduction of an external stimulus. Furthermore, quantification of ligand binding is determined by a determination of the extent of the change in the characteristics of the label.

A combination of the labeling system of Hoffman with the assay system of Reed would not have resulted in the presently claimed application. As discussed above, Reed does not teach the attachment of a label to a biological sensing element. The ordinarily skilled person would not have contemplated using the stimulus-responsive system of Hoffman with the library based assay of Reed – mainly because a significant requirement of the system of Hoffman is attachment of the stimulus-responsive component to the interactive molecule – in the case of Reed, the expressed olfactory receptor. As the olfactory receptor in Reed is expressed directly in the cell of the cell based assay, there is no way in which the stimulus-responsive component could be attached. Even if the ordinarily skilled person could have deduced a way from Reed or Hoffman to attach the stimulus-responsive component to the expressed olfactory receptor (which is doubted), the resulting system would not have been that of the presently claimed invention as the presence of the stimulus-responsive component would not allow detection of the quantity of bound ligand, but rather would only allow detachment of that ligand.

In respect of the claims specifically enumerated by the Examiner, it is also disputed that these are taught or suggested by combination of the disclosure of Hoffman with that of Reed. The Examiner understood to claim that it would have been straightforward to modify the binding analysis of Reed by modifying the binding site to contain cysteine residues (as allegedly disclosed by Hoffman) and labels to thereby

direct, control and detect binding interactions (as allegedly disclosed by Hoffman). As a first point, the olfactory receptor of Reed is expressed directly in the cell based assay system. Therefore modification of the binding site to include cysteine residues would involve mutagenesis prior to expression. This may affect expression. As a second point, Reed does not disclose attachment of a label to the expressed olfactory protein and hence introduction of cysteine residues would not advance the system of Reed. The applicants submit that the claims highlighted by the Examiner are inventive over Reed in view of Hoffman.

As for the Examiner's combination of Reed and Gold to allegedly have taught the invention of claims 26 and 27, the applicants submit that the expressed olfactory receptor of Reed does not have a label attached thereto. Thus, even if the ordinarily skilled person were to have considered using the fluorescent probes described in Gold in the system of Reed, there is nothing in Reed that teaches attachment of the label to the expressed olfactory receptor.

There is nothing in Reed, when in combination with Gold, or alone, which teaches the attachment of a detectable label to the expressed olfactory receptor (being equivalent to the biological sensing element of the present application).

It is therefore submitted that all of the claims are inventive over Reed taken in view of Gold.

Withdrawal of the Section 103 rejections are requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned in the event anything further is required.

Respectfully submitted,

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